

REMARKS

In accordance with the present invention, there are provided methods for minimizing or eliminating injury to a living system caused by cooling such living system without the formation of ice therein. Invention methods also facilitate the rapid introduction and washout of cryoprotectant fluids without toxicity or osmotic injury.

By the present communication, claims 19, 28, 31, 38, 42, 43 and 46 have been amended to define Applicant's invention with greater particularity. No new matter has been introduced by the subject amendments as the amended claim language is fully supported by the specification and original claims.

Upon entry of the amendments submitted herewith, claims 19, 21-28, 31, 32, 34-36 and 38-46 remain pending in this application and under active prosecution. A detailed listing of all claims that are, or were, in the application is presented herewith, beginning on page 2, along with an appropriate status identifier.

Rejection under 35 USC § 112, first paragraph

The rejection of claims 19, 21-28, 31-32, 34-36 and 38-46 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement, is respectfully traversed. Specifically, Applicant respectfully disagrees with the Examiner's assertion that "[t]he claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor(s), at the time the application was filed, had possession of the claimed invention." See page 2, lines 18-21 of the Office Action. Contrary to the Examiner's assertion, the ranges used in the claims to describe tonicity are clearly described in the specification in such a way as to show that Applicant had possession of the invention as claimed at the time the application was filed.

The Examiner's attention is directed, for example, to original claims 3-6, which recite tonicity ranges of 1-4, 1.1-2.7, 1.1-2 and 1.2-1.5 times isotonic, respectively. Since the original

claims are part of the specification, Applicant was clearly in possession of the invention as currently claimed at the time the present application was filed.

The Examiner's attention is also directed to Figure 4, which shows that cooling to -22°C without the formation of ice under isotonic conditions (tonicity = 1X) causes the loss of nearly 40% of the functional capacity of rabbit kidney slices as measured by the K/Na ratio. The graph indicates, however, that all tonicities between 1 and 2.2 times isotonic give rise to less injury after cooling to the same temperature in the absence of ice than is caused by cooling under isotonic conditions. There are explicit data points at 1.2, 1.5, and 2 times isotonic, all of which are between 1 and 4 times isotonic. In addition, the third paragraph of Example 6 (bridging pages 19-20 of the specification) explicitly recites 1.2 to 1.5 times isotonic as one optimal range (see especially page 19, line 30).

Figure 4, therefore, fully supports the claims by showing that, at a tonicity of 1.1 times isotonic, the recovery expected would be about 81% of control K/Na ratio, which is clearly much better than the recovery obtained when the slices were cooled under isotonic conditions. Cooling at 1.1X is projected by Figure 4 to yield recovery higher than cooling at 2.2X, and so it is clearly within the scope of the present invention. This was recognized explicitly by original claims 4 and 5, which specified ranges of 1.1 to 2.7 times isotonic and 1.1 to 2 times isotonic, respectively. The inventor was, therefore, clearly in possession of the invention, as represented by such ranges, at the time the application was filed.

The Examiner's attention is further directed to original claim 17, which provides for the presence of polymers totaling 0.1 times isotonic in order to increase the tonicity of the medium to within the optimal range (as specified by original Claim 13); if added to an isotonic solution, polymers at this concentration would produce a total tonicity of 1.1 times isotonic. This is further supported by Table 4, which specifies a tonicity of 1.1 times isotonic for LM5 plus 1% decaglycerol. The limit of 2.7 times isotonic is shown in Figure 5 to yield a recovery of nearly 70%, even after cooling to below -100°C without the formation of ice, which is superior to the

recovery obtained in Figure 4 after cooling under isotonic conditions to only -22°C. The range of 1.1 to 1.5 times isotonic is fully supported by Figure 4 and by the combination of the 1.1 to 2.7 times isotonic range of original claim 4 and the 1.2 to 1.5 times isotonic range specified in paragraph 3 of Example 6.

The range of tonicity between 1 and 4 times isotonic is supported by original claim 3 and by Example 1 (see especially page 12, lines 5-24 of the specification) where the benefits of a 4 times isotonic solution are demonstrated in experiments in which the effects of freezing were simulated without freezing. As noted in the 3rd paragraph of the Summary of the Invention, “a further embodiment is the use of [a] hypertonic medium to reduce both cryoprotectant toxicity and chilling injury, wherein the hypertonic medium is added and removed in a manner that simulates the effects of both freezing and thawing. In a further embodiment the hypertonic medium prevents cooling injury at subzero temperatures.” This language clearly indicates that 4 times isotonic solutions as described in Example 1 were envisioned at the time the invention was filed as having utility for the prevention of injury caused by cooling without the formation of ice. Clearly, tonicities as high as 4X have been demonstrated to be protective under some conditions, and numerous other tonicities between 1X and 4X have also been established to be protective (as shown in Figure 4, Figure 5, and numerous other locations in the specification (as discussed herein, and as previously detailed, for example, on page 9, 3rd paragraph, of the Amendment and Reply filed on November 11th, 2005)). In view of the extensive support referred to herein, it is respectfully submitted that the protective range between 1X and 4X is fully supported by the specification as filed.

Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph, are respectfully requested.

Rejection under 35 USC § 112, second paragraph

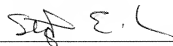
The rejection of claims 19, 21-28, 31-32, 34-36 and 38-46 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite, is respectfully traversed. Applicant respectfully disagrees with the Examiner's assertion that "the language 'otherwise caused by cooling' is unclear. . ." (see page 4, line 5 of the Office Action). The terminology at issue merely further defines the nature of the injury which is minimized or eliminated by the invention method, i.e., injury which is otherwise caused by cooling without formation of ice.

However, in efforts to reduce the issues and expedite prosecution, this rejection has been rendered moot by the deletion of all occurrences of the word "otherwise" from the claims. The resulting expression, i.e., "injury . . . caused by . . ." is respectfully submitted to be clear and unambiguous.

Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph, are respectfully requested.

In view of the above amendments and remarks, it is respectfully submitted that the pending claims are in condition for allowance. Accordingly, reconsideration and favorable action on all claims are respectfully requested. In the event any issues remain in view of this communication, the Examiner is encouraged to contact the undersigned at the telephone number listed below so that a prompt disposition of this application can be achieved.

Respectfully submitted,

By 

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